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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/308,207	05/13/1999	NIGEL DUNN-COLEMAN	GC369-2PCT	5860

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EXAMINER

WALICKA, MALGORZATA A

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 10/06/2003

16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/308,207

Applicant(s)

DUNN-COLEMAN ET AL.

Examiner

Malgorzata A. Walicka

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 July 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 19-40 is/are pending in the application.
- 4a) Of the above claim(s) 32-40 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 19-31 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☒ The proposed drawing correction filed on 10 July 2003 is: a) ☒ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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The Amendment and Response to Office Action filed on July 10, 2003 is acknowledged. The amendments to the specification and claims have been entered as requested.

Claims 1-18 are cancelled. Claims 19-40 are pending. Claims 19-31 are the subject of this Office Action. Claims 32-40 are withdrawn from consideration by the examiner, 37 CFR 1.142(b), as being drawn to the non-elected invention; see the previous Office Action, paper No. 13.

Detailed Office Action

1.1. Objections

1.1. Abstract

The submission of the new Abstract describing the invention as now claimed is acknowledged.

1.2. Drawings

Applicants' corrections to Figure 9 and 10 are accepted by examiner.

1.3. Disclosure

The objection to disclosure for use of the symbol ® in equations 1, 2, 3, 4, on pages 1 and 2 is withdrawn because the proper corrections have been entered.

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The objection to the specification because the description of protein X is indefinite is withdrawn in the light of Applicants arguments.

The correction of the address of the American Type Culture Collection on page 9, line 34 is noted.

1.4. Claims

The examiner noted correction of the spelling error in claim 24.

2. Rejections

2.1. 35 U.S.C. section 112, second paragraph

Rejection of claims 19 and 20 and dependent claims 21-23 for indefiniteness of the terms protein X, protein 1, protein 2 and protein 3 is withdrawn in the light of Applicants' arguments.

Rejection of claim 28 is withdrawn because the sequence identification number SEQ ID NO: 59 has been cancelled.

Rejection of amended claims

Claim 21 is confusing in recitation of the phrase "The recombinant microorganism of Claim 19 selected from the group consisting of *Citrobacter*, *Enterobacter*, etc." Claim 21 is examined assuming that the host cells used for transformation were the species belonging to the recited genera.

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Claim 28 is rejected, because the phrase "as shown between positions 0749 – 1157 of SEQ ID NO: 19" is confusing. The examiner proposes "consisting o nucleotides 9749-11572 of SEQ ID NO: 19."

Claims 29-31 recite the limitations "protein 1", "protein 2" and "protein 3". There is insufficient antecedent basis for this limitation in the claim, because the base claim 20 does not recite "protein 1", "protein 2" and "protein 3".

Claim 19-30 are confusing because the base claim 19 is directed to a recombinant microorganism comprising a) at least one gene encoding a dehydratase activity, b) at least one gene encoding a glycerol–3 phosphatase and c) at least one gene encoding protein X. It is unknown whether the host cell used for production of the recombinant microorganism has these genes as native or they were introduced. For examining it is assumed that the genes were introduced into the microorganism to make it a recombinant microorganism.

2.2. 35 U.S.C. section 112, first paragraph paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2.2.1. Lack of written description

Claims 19-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter,

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which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are generic, because they are directed to a large and variable genus of recombinant microorganisms transformed with the following subgenera of genes:

- a) any gene encoding a dehydratase activity,
- b) any gene encoding a glycerol-3 phosphatase, and
- c) any gene encoding protein X, wherein protein X has at least 50% similarity to protein X encoded by nucleotides 9749-11572 of SEQ ID NO:19 or protein X encoded by ORF of the dha regulon of the genus of *Citrobacter*.

In case of subgenera a) and b) the claims are missing description of structure of the genes used for transformation or other identifying characteristics of such genes. It is not clear which of extremely large number of dehydratases and glycerol-3 phosphatases produced by living organism or man-made are included or excluded from the scope of invention. In addition, one skilled in the art may instantly note that of many kinds of dehydratases, from any source, the diol or glycerol dehydratases should be used for making the claimed invention.

Regarding subgenus c) the claims do not recite the function and structure of protein X wherein said protein X has at least 50% similarity to protein X encoded by nucleotides 9749-11572 of SEQ ID NO: 19 or protein X encoded by ORF of the dha regulon of the genus of *Citrobacter*. The subgenus c) encompasses an extremely large

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number of DNA molecules for which the function is not stated in the claims. Two representatives of this large number of species, i.e. nucleotides 9749-11572 of SEQ ID NO: 19 or DNA encoding protein X encoded by ORF of the dha regulon of the genus of *Citrobacter*, do not provide sufficient structural characteristics to identify every species in the genus. Providing these two species is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Applicants fail to disclose any particular structure to function/activity relationship for polynucleotide 9749-11572 of SEQ ID NO: 19 or DNA molecule encoding protein X encoded by ORF of the dha regulon of the genus of *Citrobacter*. No information, beyond the quotation of nucleotides 9749-11572 of SEQ ID NO: 19 and DNA encoding protein X encoded by ORF of the dha regulon of the genus of *Citrobacter*, has been provided by Applicants, which would indicate that they had possession of the claimed genus of these modified polynucleotides. The specification does not contain any disclosure of the nucleotide sequences derived from nucleotides 9749-11572 of SEQ ID NO: 19 or DNA encoding protein X encoded by ORF of the dha regulon of the genus of *Citrobacter*, by substitution, deletion or addition one or more nucleotides to obtain DNA molecules having 50% and more identity to the initial sequences. The specification fails to teach how to modify initial nucleotide sequences so that the encoded protein retained the function of protein X. Thus, predictability of the function of the representatives of the claimed genus is not apparent.

Federal Circuit states that the primary function of the written description requirement is to insure that an inventor had possession of the claimed subject matter

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and to allow one skilled in the art to recognize what is claimed. *See in re Blaser*, 556 F.2d 534, 194 U.S. P. Q. 122 (CCPA 1977), *Enzo Biochem*, 285 F. 3d 1013, 62 U.S.P.Q.2d 1289. The written description requirement is satisfied by the disclosure of the claimed subject matter in such a descriptive means, e.g., words, structures, figures and diagrams, to allow one skilled in the art to visualize or recognize the claimed subject matter, *Enzo Biochem*. 285 F. 3d 1013.”

One skilled in the art is not able to visualize or recognize the invention because the claimed subject matter is not disclosed in such descriptive means as structures, or figures presenting such structures or even words presenting details of structures listed under c) above.

In addition, claims 20 and 29-31 are rejected because the claims do not recite the function of proteins of SEQ ID NO: 60, 61, 62 63, 64 and 65.

Furthermore, claim 20 is directed to a large and variable genus of recombinant microorganisms comprising any of the following genera:

- a) gene encoding a protein having at least 50% similarity to the protein of SEQ ID NO: 60,
- b) gene encoding a protein having at least 50% similarity to the protein of SEQ ID NO: 61,
- c) gene encoding a protein having at least 50% similarity to the protein of SEQ ID NO: 62,
- d) gene encoding a protein having at least 50% similarity to the protein of SEQ ID NO: 63,

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- e) gene encoding a protein having at least 50% similarity to the protein of SEQ ID NO: 64, and
- f) gene encoding a protein having at least 50% similarity to the protein of SEQ ID NO: 64.

The claim does not recite the function of proteins of SEQ ID NOs: 60, 61, 62, 63, 64 and 65, also the subgenera a)-f) encompass an extremely large number of DNA molecules for which the function and structure are not set forth in the claims. The representatives of this large number of species, i.e. DNA molecules encoding amino acid SEQ ID NOs: 60, 61, 62, 63, 64 and 65 do not provide sufficient structural characteristics to identify every species in the genera a)-f). Providing one DNA molecule per subgenus is insufficient to put one of skill in the art in possession of the attributes and features of all species within the subgenus. Applicants fail to disclose any particular structure to function/activity relationship for polynucleotide encoding amino acid SEQ ID NOs: 60, 61, 62, 63, 64 and 65. The specification does not contain any disclosure of the nucleotide sequences derived from nucleotides encoding amino acid SEQ ID NOs: 60, 61, 62, 63, 64 by substitution, deletion or addition of one or more nucleotides to obtain DNA molecules having 50% and more identity to the initial sequences. The specification fails to teach how to modify initial nucleotide sequences so that the encoded protein retained the functions of protein of SEQ ID NOs: 60, 61, 62, 63, 64 and 65. Thus, predictability of the function of the species of the claimed genera is not apparent.

Federal Circuit states that the primary function of the written description requirement is to insure that an inventor had possession of the claimed subject matter and to allow one skilled in the art to recognize what is claimed. *See in re Blaser*, 556 F.2d 534, 194 U.S. P. Q. 122(CCPA 1977), *Enzo Biochem*, 285 F. 3d 1013, 62 U.S.P.Q.2d 1289. The written description requirement is satisfied by the disclosure of the claimed subject matter in such a descriptive means, e.g., words, structures, figures and diagrams, to allow one skilled in the art to visualize or recognize the claimed subject matter, *Enzo Biochem*. 285 F. 3d 1013."

One skilled in the art is not able to visualize or recognize the invention because the claimed subject matter is not disclosed in such descriptive means as structures, or figures presenting such structures or even words presenting details of structures listed under a)-f) above.

Given the lack of structural and/or functional characteristics of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention when the application was filed.

2.2.2. *Scope of enablement*

Claim 19-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for microorganisms transformed with DNA molecule consisting of nucleotides 9749-11572 of SEQ ID NO: 19 and DNA molecule encoding

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protein X encoded by ORF of the dha regulon of the genus of *Citrobacter*, does not reasonably provide enablement for microorganism transformed with DNA encoding protein X that has at least 50% similarity to protein X encoded by nucleotides 9749-11572 of SEQ ID NO: 19 or protein X encoded by ORF of the dha regulon of the genus of *Citrobacter*.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The claims are broader than the enablement provided by the disclosure with regard to the extremely large number of microorganisms transformed with polynucleotides encoding protein X that has at least 50% similarity to protein X encoded by nucleotides 9749-11572 of SEQ ID NO:19 or protein X encoded by ORF of the dha regulon of the genus of *Citrobacter*, see the above rejection for lack of written description.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Otherwise, undue experimentation is necessary to make the claimed invention. Factors to be considered in determining whether undue experimentation is required, are summarized *In re Wands* [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the nature of the invention, (b) the breadth of the claim, (c) the state of the prior art, (d) the relative skill of those in the art, (e) the predictability of the art, (f) the presence or absence of working example, (g) the amount of direction or guidance presented, (h) the quantity of experimentation necessary.

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The nature and breath of the claimed invention encompasses any microorganism that is transformed with at least one DNA encoding:

- 1) protein X that has at least 50% similarity to protein X encoded by nucleotides 9749-11572 of SEQ ID NO: 19 or
- 2) protein X that has at least 50% similarity to protein X encoded by ORF of the dha regulon of the genus of *Citrobacter*.

While methods of gene cloning and gene structure manipulations are well known in the relevant art, and skills of the artisans highly developed, no one is able to make a transformant transformed with polynucleotide enumerated under (1) –(7) above, because the lack of functional and structural characteristics of said polynucleotides makes the probability of success in obtaining the claimed invention very low. The claims necessitate selecting of DNA molecules that supposedly encode

- 1) protein X that has at least 50% similarity to protein X encoded by nucleotides 9749-11572 of SEQ ID NO: 19 or
- 2) protein X that has at least 50% similarity to protein X encoded by ORF of the dha regulon of the genus of *Citrobacter*,

sequencing them, selecting those that have property 1) or 2), expressing them in an appropriate host and selecting those that act as protein X. While enablement is not precluded by a tedious experimentation, such experimentation has low probability of success absent teachings regarding the structure of the DNA molecules used for transformation or a guidance how to modify the initial DNA molecules so that after modification they retained the desired property of encoding protein X and 50% similarity

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to its original amino acid sequence.

Examiner concludes that without the further guidance on the part of Applicants regarding function and structure of the polynucleotides used for transformation, experimentation left to those in the art is improperly extensive and undue.

Claim 20 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for microorganisms transformed with DNA molecule encoding polypeptides SEQ ID NO: 60, 61, 62, 63 64 and 65, does not reasonably provide enablement for microorganism transformed with DNA molecules encoding proteins that are in at least 50% similar to polypeptides of SEQ ID NO: 60, 61, 62, 63, 64 and 65. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are broader than the enablement provided by the disclosure with regard to the extremely large number of microorganisms transformed with polynucleotides encoding polypeptides having at least 50% similarity to polypeptides of SEQ ID NO: 60, 61, 62, 63 64 and 65; see the above rejection for lack of written description.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Otherwise, undue experimentation is necessary to make the claimed invention. Factors to be considered in determining whether undue experimentation is required, are summarized *In re Wands*

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[858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the nature of the invention, (b) the breadth of the claim, (c) the state of the prior art, (d) the relative skill of those in the art, (e) the predictability of the art, (f) the presence or absence of working example, (g) the amount of direction or guidance presented, (h) the quantity of experimentation necessary.

The nature and breath of the claimed invention encompasses any microorganism that is transformed with at least one DNA encoding:

- a) a protein having at least 50% similarity to the protein of SEQ ID NO: 60,
- b) a protein having at least 50% similarity to the protein of SEQ ID NO: 61,
- c) a protein having at least 50% similarity to the protein of SEQ ID NO: 62,
- d) a protein having at least 50% similarity to the protein of SEQ ID NO: 63,
- e) a protein having at least 50% similarity to the protein of SEQ ID NO: 64, and
- f) a protein having at least 50% similarity to the protein of SEQ ID NO: 64.

While methods of gene cloning and gene structure manipulations are well known in the relevant art, and skills of the artisans highly developed, no one is able to make a transformant transformed with polynucleotide enumerated under (1) –(7) above, because the lack of the functional and structural characteristics of said polynucleotides makes the probability of success in obtaining the claimed invention very low. The claims necessitate selecting, from all natural or man made sources, DNA molecules that supposedly encode

- a) a protein having at least 50% similarity to the protein of SEQ ID NO: 60,
- b) a protein having at least 50% similarity to the protein of SEQ ID NO: 61,

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c) a protein having at least 50% similarity to the protein of SEQ ID NO: 62,
d) a protein having at least 50% similarity to the protein of SEQ ID NO: 63,
e) a protein having at least 50% similarity to the protein of SEQ ID NO: 64, and
f) a protein having at least 50% similarity to the protein of SEQ ID NO: 64,
sequencing them, selecting those that have property a)-f), expressing them in an appropriate host and selecting those that act as proteins of SEQ ID NO: 60, 61, 62, 63, 64 or 65. While enablement is not precluded by a tedious experimentation, such experimentation has low probability of success absent teachings regarding the structure of the DNA molecules used for transformation or guidance how to modify the initial DNA molecules so that after modification they retained the desired property of encoding proteins having the same functions of the same as those of amino acid sequence of SEQ ID Nos: 60, 61, 62, 63, 64, 65 and 50% similarity to the original amino acid sequence.

Examiner concludes that without the further guidance on the part of Applicants regarding function and structure of the polynucleotides used for transformation, experimentation left to those in the art is improperly extensive and undue

2.3. Double patenting rejection

Statutory and nonstatutory double patenting rejection of claims 1-8 is moot because the claims have been cancelled.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka, Ph.D., whose telephone number is (703) 305-7270. The examiner can normally be reached Monday-Friday from 10:00 a.m. to 4:30 p.m.

If attempts to reach examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, Ph.D. can be reached on (703) 308-3804. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionists whose telephone number is (703) 308-0196.

Malgorzata A. Walicka, Ph.D.

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Patent Examiner


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